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Determinants of immunological failure among clients on the first line treatment with highly active antiretroviral drugs in Dar es Salaam, Tanzania

Anthony Kapesa[1,2*], Daniel Magesa[1,3], Alexander William[1], John Kaswija[4], Jeremiah Seni[5], Cyprian Makwaya[6]

[1]*Department of Community Medicine, Muhimbili University of Health and Allied Sciences, P.O. Box 65007, Dar es salaam, Tanzania*

[2]*Department of Community Medicine, Catholic University of Health and Allied Sciences, P.O. Box 1464, Mwanza, Tanzania*

[3]*Pastoral Activities and Services for People with AIDS Dar es Salaam Archdiocese, P.O. Box 70225, Dar es Salaam, Tanzania*

[4]*Zonal Health Resource Centre-Tanzania Ministry of Health and Social Welfare P.O. Box 11351, Mwanza, Tanzania*

[5]*Department of Microbiology and Immunology, Catholic University of Health and Allied Sciences, P.O. Box 1464, Mwanza, Tanzania*

[6]*Department of Epidemiology and Biostatistics, Muhimbili University of Health and Allied Sciences, P.O. Box 65007, Dar es salaam, Tanzania*

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ABSTRACT

Objective: To determine socio-cultural, demographic and highly active antiretroviral therapy (HAART) program-related factors associated with immunological failure (IF) among clients on HAART in Dar es Salaam care and treatment clinics.

Methods: A 1:2 matched case control study was done from February to April 2012 in HIV/AIDS care and treatment clinics in Dar es Salaam. Data were collected from National AIDS Control Program (NACP) data base and patient's charts to obtain 60 sets of study participants who were interviewed using the structured questionnaire. Data analysis was done by using EPI Info 3.5.1 version.

Results: The mean age of all study participants was (42.00±9.07) years with 35% (63) being males. History of poor antiretroviral therapy (ART) adherence due to exposure to drug holiday with loss to follow up (OR=11.96; 95% *CI*=2.07-69.26), history of changing care and treatment clinics (OR=12.07; 95% *CI*=2.10-69.27) and the lack of treatment supporter (OR=23.26; 95% *CI*=1.85-291.66) were found to be strongly associated with the occurrence of first line HAART-IF.

Conclusions: HAART-IF in Dar es Salaam is associated with ART programmatic and patients' centered challenges. There is a need to review the approaches on ensuring ART adherence, clients follow up and referral system so as to reduce the incidence of IF as we move to a more decentralized peripheral drug picks clinical initiative.

1. Introduction

Africa South of Sahara is still the World's most highly affected region with HIV/AIDS and accounts for approximately 70% of the global disease burden[1]. It is now about ten years since the commencement of antiretroviral therapy (ART) scales up in most parts of this continent but only 40% of those who need the service are reached[2]. Care and treatment to people living with HIV/AIDS (PLHIV) has improved the outcome of the disease in both developed and developing countries by reducing significantly the mortality rates[3-8].

Rapid scale up of ART services in Tanzania together with other parts of Africa face challenges which affect the delivery of the expected services to people in need. These includes shortages of skilled and experienced personnel; lack of sustainable funding; low coverage in rural settings; low socioeconomic status among PLHIV; effects of stigma; ART adherence issues; ART drug resistance and immunological failure (IF) among people on highly active antiretroviral therapy (HAART)[9-12].

*Corresponding author: Dr. Anthony Kapesa, Department of Community Medicine, Muhimbili University of Health and Allied Sciences, P.O. Box 65007, Dar es salaam, Tanzania.
Tel: +255766 379446
E-mail: anthony1kapesa@gmail.com
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Treatment IF is a state where the clients who have been on ART experience 50% drop of the CD4 count or return to the baseline count in six month with a history of good adherence to treatment[13].

Studies in East Africa show a high prevalence of IF ranging from 8% to 57% among clients on first line HAART and furthermore the magnitude increases as the time of follow up increases[14-16]. It is well known that virological failure is a better marker of HAART failure as opposed to IF[14], but financial constraints hinder universal access to this method in many resource limited settings like Tanzania making IF a pivotal marker not only to predict virological failure but also to guide change of the treatment regimen.

Non adherence to treatment has been reported to be major cause of IF[14,16], whereas stigma, food security, social support, income and tuberculosis co-morbidity have been reported to affect ART adherence[15,17-20]. Despite evidence from other areas on the socio-cultural and demographic factors as well as HAART program-related challenges which partly or wholly result into treatment IF, little is known among HIV/AIDS clients attending care and treatment clinics (CTC) in Dar es Salaam, Tanzania.

2. Materials and methods

2.1. Study design and sampling process

A 1:2 matched case control study was conducted at Mwananyamala, Temeke, Mnazi Mmoja and Mbagala Hospitals in Dar es Salaam from February to April 2012 in HIV/AIDS CTC. Data collection process used the National AIDS Control Program (NACP) data base together with patient's charts to sort 180 study participants [60 qualified cases of IF and 120 controls (without IF)]. The study cases were the clients on first line HAART for at least one year with immunological failure (50% drop of the CD4 count from the peak value in six month or return to the baseline CD4 count). The study controls were clients on the first line HAART for at least one year of follow up with good treatment immunological response (*i.e.* clients without any history CD4 count drop of more than 25% in a period of six month). The obtained cases were matched with two controls by using sex, age group, baseline CD4 count and ART follow up time as matching variables.

2.2. Data collection techniques and tools

The data was collected by using a structured questionnaire administered equally to both cases and control. Data pertaining to social demographic variables, ART baseline information, adherence, stigma assessment, history of ART loss to follow up, HIV co-morbidity, self-reported food security, nutrition, income and social support were inquired. The measurement of HIV related stigma was made by using three important parts of Berger's scale of HIV stigma[21]. The scores were given using Likert's scale (strongly agree; agree; disagree; strongly disagree) with a score range of 16-64 points as a minimum to the maximum. The study members with scores less 32 were considered less stigmatized and individuals with the scores more than or equal to 32 were considered as more stigmatized. History of adherence to antiretroviral drugs for the past six month was sought basing on patient clinical files and self-reporting. Any history of adherence of less than 95% was considered poor. Assessment of food security was based on physical and financial accessibility foods throughout the year and three-day nutritional history was taken. The income of less than one USD per person per day in the family was considered as exposure to low income.

2.3. Data analysis

Data pertaining to socio-demographic characteristics, ART baseline information, adherence status, stigma, food security and other variables were entered into Excel sheet®, cleaned and exported to Epi info software version 3.5.1 for analysis according to the objectives of the study. Frequency distribution of the socio-demographic characteristics were described and compared the cases with the controls. The bivariate analysis using maximum likelihood estimates of the categorical variables was done using a cross tabulation of the cases and the controls to determine the association of the variables. Odds ratio was calculated with their respective confidence interval. Furthermore, the variables with $P<0.05$ in the bivariate analysis were subjected to conditional logistic regression to get the independent predictors of IF measured by adjusted odds ratio (aOR) together with their respective confidence interval.

2.4. Study clearance and ethical considerations

The study ethical clearance was obtained from the Institutional Review Board (IRB) of the Muhimbili University of Health and Allied Sciences. A written informed consent from each ART client was sought and confidential handling of clinical information was carefully observed by using anonymous codes.

3. Results

Of all study participants 63 (35%) were males whereas 21 (33.33%) of all study cases with IF were males. More than two third of the study population aged between 31 and 50 with the overall mean age of (42.00±9.07) years. Furthermore, 79 (43%) were married with more than one third being petty traders with primary school education (Table 1).

Bivariate analysis found an association between IF and prior history of CTC change (aOR=7.09, 95% *CI*=3.18-17.59), HIV stigma (aOR=2.52, 95% *CI*=1.27-5.23), limited HIV status disclosure (aOR=3.11, 95% *CI*=1.19-9.53) and lack of disclosure of the HIV status to the family members (aOR=3.49, 95% *CI*=1.59-8.34). Moreover, IF was also associated with negative public attitude about people living with HIV (aOR=3.35, 95% *CI*=1.59-7.60), history of poor ART adherence in six month (aOR=13.11, 95% *CI*=4.29-55.24) and ART poor adherence in past one year (aOR=13.74, 95% *CI*=5.21-45.79). Furthermore, bivariate analysis also found a strong association between IF and exposures to ART drug holidays with loss to follow up (aOR=9.55, 95% *CI*=3.87-27.49) and lack of treatment supporter (aOR=26.79, 95% *CI*=7.49-167.12) (Table 2).

Upon conditional logistic regression analysis, exposure to drug holiday which is associated with ART loss to follow up (OR=11.963 1; 95% *CI* 2.06-69.25), history of changing CTC (OR=12.072 2; 95% *CI* 2.10-69.27) and lack of treatment supporter(OR=23.256 6; 95% *CI* 1.85-291.68) were found to be independent predictors of the occurence of first line HAART-IF (Table 3).

Table 1

Social demographic characteristics of the study participants.

Variable		Case [*n* (%)]	Control [*n* (%)]	Total [*n* (%)]	*Chi*-square**	*P*-value
Age (years)	≤30	9 (40.91)	13 (59.09)	22 (100)		
	31-40	19 (31.15)	42 (68.85)	61 (100)	0.829 6	0.842*
	41-50	20 (31.75)	43 (68.25)	63 (100)		
	≥51	12 (35.29)	22 (64.71)	34 (100)		
Sex	Male	21 (33.33)	42 (67.67)	63 (100)		
	Female	39 (33.33)	78 (67.67)	117 (100)	0.000 0	1.000*
Marital status	Married	24 (30.38)	55 (69.62)	79 (100)		
	Never married	7 (26.92)	19 (73.08)	26 (100)		
	Widowed	9 (32.14)	19 (67.86)	28 (100)	2.600 0	0.630
	Cohabiting	3 (42.86)	4 (57.14)	7 (100)		
	Divorced	17 (42.50)	23 (57.50)	40 (100)		
Education	No formal education	1 (8.30)	11 (91.70)	12 (100)		
	Primary	42 (33.10)	85 (66.90)	127 (100)		
	Secondary	10 (33.30)	20 (66.67)	30 (100)	9.370 0	0.520
	College	5 (55.60)	4 (44.40)	9 (100)		
	University	2 (100)	0 (0.00)	2 (100)		
Occupation	Peasant	5 (38.46)	8 (61.54)	13 (100)		
	Petty trader	17 (29.31)	41 (70.69)	58 (100)		
	Business	12 (34.29)	23 (65.71)	35 (100)	1.900 0	0.860
	Employment	16 (35.56)	29 (64.44)	45 (100)		
	House wife	6 (28.57)	15 (71.43)	21 (100)		
	Unemployed	4 (50.00)	4 (50.00)	08 (100)		

*: Matched variables; **: Fisher's exact was used where appropriate.

Table 2

Bivariate analysis of the first line HAART immunological failure by exposure variables.

Exposure variable	MLE (aOR)	95% *CI*	Exact mid-*P* (*P*-value)
Alcohol use	1.00	0.43-2.27	0.495
History of CTC change	7.09	3.18-17.59	<0.001
Berger`s HIV stigma	2.52	1.27-5.23	0.004
Unprotected sex	3.35	1.24-9.83	0.008
PITC mode of CTC entry	1.22	0.65-2.32	0.267
Unsatisfactory diet	1.00	0.45-2.14	0.495
Limited disclosure	3.11	1.19-9.53	0.009
Insufficient income to carter for food	1.78	0.78-4.06	0.085
Living with a sexual partner	1.48	0.41-5.17	0.266
Negative self-image	3.78	0.94-18.46	0.029
Post exposure prophylaxis	2.16	0.62-7.79	0.112
Public attitude about people living with HIV	3.35	1.59-7.60	<0.001
Adherence below 95% in six month	13.11	4.29-55.24	<0.001
Lack of treatment supporter	26.79	7.49-167.12	<0.001
ART straight forward	1.34	0.46-4.42	0.309
HIV status disclosure after six month	2.32	0.96-6.08	0.036
ART poor adherence in past one year	13.74	5.21-45.79	<0.001
History of TB infection	2.00	0.21-19.21	0.259
Drug holiday with loss to follow up	9.55	3.87-27.49	<0.001
Lack of family disclosure	3.49	1.59-8.34	<0.001
No disclosure to the sexual partner	1.09	0.54-2.18	0.406
Personal income of less than one USD per day	0.84	0.29-2.34	0.390

Table 3

Conditional logistic regression of IF predictor variables

Exposure variable	*OR*	95% *CI*	*P*-value
History of change of CTC point	12.072 2	2.10-69.27	0.005
Berger's HIV stigma	0.064 8	0.00-2.82	0.155
Unprotected sex	1.287 0	0.08-20.41	0.858
Limited disclosure	1.839 3	0.15-23.18	0.637
Drug holiday	11.963 1	2.06-69.25	0.006
Limited family disclosure	1.126 5	0.27-4.64	0.869
Negative self image	0.932 0	0.02-36.12	0.969
Negative public attitude	28.157 1	0.62-1286.59	0.087
Six month poor adherence	3.220 9	0.06-161.39	0.558
HIV status disclosure after six month	1.897 8	0.19-18.61	0.582
Lack of treatment supporter	23.256 6	1.85-291.68	0.015
ART poor adherence in past one year	4.666 3	0.27-81.27	0.290

4. Discussion

This study compared various demographic variables among patients attending CTC on the immunological outcome and found not any significant difference between the case and control groups. Poor adherence to ART was strongly associated with IF in the present study, whereas both IF and virological failure were also associated with poor adherence in other studies[16,19,22]. HIV related stigma remains one of the challenges facing Sub Saharan ART programs. This study revealed an association in the overall Berger's HIV stigma, disclosure concerning factors and perception on public attitude about PLHIV and subsequent IF among the first line HAART clients at the bivariate analysis. Studies in Sub Saharan Africa have shown how HIV stigma has contributed to not only to poor ART adherence but also affecting the ART health

seeking behavior among PLHIV[23-25]. The present study showed that the changes in CTC clinics and exposure to drug holidays are strongly associated with IF. Problems related to ART loss to follow up clients and its effect in the performance of ART program was also shown in another study in Malawi[26]. The aforementioned constrains emphasize the need to strengthen the CTC tracking system and thus maximize retention rates among the clients on HAART. Furthermore, we speculate that loss to follow up may partly be attributing to the escalating burden of HIV1 drug resistance as shown in the two recent sub-Saharan Africa studies with Uganda (12.3%) and Tanzania (14.8%) showing the highest prevalence among treatment naive patients[27,28]. In the light of these findings, one of factors which may cause high rate HAART resistance in Tanzania as shown in the Mwanza study[28], could be the fact that some of the study participants were possibly not truly HAART naive but rather they had been exposed to antiretroviral drugs and due to frequent changes in CTC, they may undisclosed the information and thus re-registered as new clients.

The conditional logistic regression analysis of socio-economic variables showed that lack of ART treatment supporter among the first line HAART clients was strongly associated with IF. This finding is in consistent with another similar study which finds an association between social support and prescribed drug adherence[29]. Furthermore, positive social supports, including being married and family support have clearly been associated with adherence to ART as many studies from different parts of the world[18,30-33].

Though not shown in the present study, many studies in sub-Saharan Africa have shown that food insecurity contributes to poor ART adherence and subsequent undue treatment outcome among these HIV patients on HAART[20,34,35]. Other studies in sub-Saharan Africa have reported high inconsistence in condom use and tendency to underreport issues pertaining to sexuality among client on HIV care and treatment, situations which may mislead a truly behavioral picture regarding IF as shown in the present study[36-39].

Lack of viral load measurements in this study due to financial constraints could have been of interest so as to further delineate its contribution to IF.

Immunological failure among patients on HAART attending CTC in Dar es Salaam is due to both ART programmatic and patients' centered challenges with poor adherence to HAART due to exposure to drug holiday with loss to follow up, history of changing of CTC and the lack of treatment supporter being independent predictors of IF. There is a need to review the approaches on ensuring ART adherence, clients follow up and referral system so as to reduce the incidence of immunological failure as we move to a more decentralized peripheral drug pick clinical initiative.

Conflict of interest statement

We declare that we have no conflict of interest.

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